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Original Research Paper

EVALUATING THE FUNCTION OF THE SPLEEN IN INDIAN CHILDREN WITH SICKLE CELL DISEASE

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ABSTRACT

Background: Chronic haemolytic anaemia with episodic acute consequences that cause increasing damage to important organs is known as sickle cell disease (SCD).

Aim: The purpose of this study was to evaluate the frequency and determinants of splenic dysfunction in children with sickle cell disease from India.

Methods: This study evaluated 132 children with sickle cell disease, ages 1 to 15, and checked for splenic dysfunction. The size of each subject's spleen was measured by clinical examination and ultrasound. Technetium-99m (99mTc) tagged autologous RBCs were used to measure spleen dysfunction by looking for Howell Jolly bodies in a peripheral smear. The clinical and laboratory predictors of splenic dysfunction were evaluated using multiple logistic regression.

Results: 4.6% (n=6) and 19.7% (n=26) of the research participants had absent or impaired splenic function as determined by 9mTc scintigraphy, respectively. 7.5% (n=10) of the kid participants had Howell Jolly bodies in their peripheral smears, whereas all 10 had splenomegaly and three had aberrant scintigraphy uptake. HbS > 70%, reticulocyte count > 4%, children not taking hydroxyurea, > 5 blood transfusions, > 3 previous hospitalization events, > 4 vaso-occlusive crisis (VOC) episodes, and age > 5 years were independent predictors of splenic dysfunction seen in the research.

Conclusion: According to the current study, splenic dysfunction is common in Indian kid participants, and these children might receive tailored antibiotic prophylaxis. HbS > 70%, reticulocyte count > 4%, children not taking hydroxyurea, > 5 blood transfusions, > 3 previous hospitalization events, > 4 vaso-occlusive crisis (VOC) episodes, and age > 5 years are indicators of splenic dysfunction in Indian children.

Keywords: Howell Jolly bodies, Splenectomy, splenic dysfunction, Sickle cell disease

INTRODUCTION

Chronic hemolytic anemia with episodic acute consequences that cause increasing damage to essential organs is known as sickle cell disease, or SCD. According to the extensive research on the effects of SCD as hyposplenism in babies, the spleen is one of the organs most frequently targeted in SCD patients and is impacted early.

Young children with sickle cell illness typically have a sequestration crisis due to splenomegaly and elevated splenic red pulp activity, which may occur along with function loss. By mid-

childhood, however, splenic atrophy and auto-splenectomy are the results of recurrent bouts of numerous splenic infarcts and vaso-occlusion.[1]

Loss of splenic function raises the risk of infection with encapsulated organisms that have high death rates. According to data from Western nations, sickle cell disease patients experience an early start of splenic dysfunction. However, it has been demonstrated that splenic dysfunction develops later in life in people from Asia, the Middle East, and Africa. A few variables, such as the usage of HU, chronic red cell transfusions, and the presence of alpha thalassemia, have shown positive impacts in terms of preserving splenic function.[2]

Determining the risk factors for individuals with splenic dysfunction is essential for lowering the threshold for infection suspicion and treatment. Additionally, it might aid in determining whether penicillin preventative prophylaxis is necessary. The frequency of splenic dysfunction in children with sickle cell disease in India is not well documented in the literature.[3]

In order to evaluate the predictors, prevalence, laboratory results, and clinical characteristics of splenic dysfunction in Indian children with sickle cell disease, the current study was conducted.

MATERIALS AND METHODS

This study was designed to evaluate the clinical characteristics, laboratory results, prevalence, and predictors of splenic dysfunction in Indian children with sickle cell disease. Prior to their involvement in the study, all individuals gave their written and verbal informed consent.

The research evaluated 132 children with sickle cell disease, aged 1 to 15 years, of both sexes, based on high-performance liquid chromatography results showing homozygous HbSS and HbS >50%. Subjects with cancer, celiac disease, chronic liver disease, diabetes mellitus, nephrotic syndrome, tuberculosis, immunological deficiencies, congenital malformations, diseases that could impair spleen function, splenectomized subjects, and subjects whose parents did not give their consent to participate in the study were excluded from the study.

All research participants underwent a thorough clinical evaluation after their final inclusion, which was followed by a thorough history taking. A premade organized proforma was used to collect data on a variety of problems, including hydroxyurea intake, mean hemoglobin, the number of blood transfusions received, hospitalization-related infections, and VOC (vaso-occlusive crisis).

In the event that patients experienced any disease-related complications, needed a blood transfusion for congestive heart failure, or had hemoglobin levels below 5 g/dL, hospitalization was recommended. Ultrasonography and clinical evaluation were used to determine the size of the spleen. Two radiologists performed the measurements.

Paired blood cultures, HJB (Howell Jolly bodies) on peripheral blood smear examination, RBC (red blood cell) indices, and CBC (complete blood counts) were among the laboratory data evaluated. When Howell Jolly bodies were found in a subject's peripheral smear, it was determined that there were several cells per 1000 RBCs, with a count of more than 665/106 RBCs being indicative of asplenia. 5 Splenic function was also evaluated by scintigraphy using autologous

RBCs tagged with Technetium-99m (99mTc). After administering stannous pyrophosphate intravenously for 10–20 minutes, 5-8 ml of blood was drawn in a syringe protected with 99 m Tc.

The youngster was then given an injection of tagged red blood cells after they had been cooked to 49.5°C in a water bath for 20 minutes. Six planar pictures were obtained utilizing the SPECT CT anterior detector within an hour of injection. Based on the spleen's patchy or non-visible uptake, uptake less than the liver, and uptake equal to the liver, splenic function was categorized as missing, reduced, and normal. From hospital records and the individuals' histories, clinical events such as the requirement for hospitalization, blood transfusions, sequestration crises, painful crises, and serious infections were collected.

In order to evaluate descriptive measures, multiple logistic regression, and the Chi-square test, the collected data was statistically analyzed using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA). The results were expressed as mean and standard deviation and frequency and percentages. The p-value of <0.05 was considered statistically significant.

RESULTS

The current study sought to evaluate the clinical characteristics, laboratory results, prevalence, and predictors of splenic dysfunction in Indian children with sickle cell disease. In this study, 132 children with sickle cell disease, ages 1 to 15, were evaluated and tested for splenic dysfunction.

In the research, there were 51.5% (n=68) females and 48.4% (n=64) men. 36.3% (n=48) of the participants were between the ages of 1 and 5, and 67.6% (n=84) were females between the ages of 6 and 15. Hospitalization, severe infections, vaso-occlusive crises, and blood transfusions were reported in 74.25% (n=98), 21.21% (n=28), 92.43% (n=122), and 83.3% (n=110) of the research participants, respectively. The following symptoms were present in 6.06% (n=4), 13.64% (n=18), 9.09% (n=12), 4.55% (n=6), 36.3% (n=48), 22.7% (n=30), 34.8% (n=46), 62.1% (n=82), and 63.6% (n=84) of the subjects: stroke, dyspnea, chest pain, hematuria, anemia, jaundice, stomach discomfort, fever, and acute painful crises (Table 1).

According to the national immunization schedule, 100% of the study participants (n=132) received vaccinations, and 3% (n=4) received penicillin prophylaxis. Meningococcal, pneumococcal, and H. influenza B vaccinations were given to 7.6% (n=10), 12.1% (n=17), and 34.9% (n=46) of the patients in the optional vaccination history, respectively. In 1.5% (n=2), 1.5% (n=2), 1.5% (n=2), 3% (n=4), 6% (n=8), and 7.5% (n=10) of the research participants, the infection types were Hepatitis B, abscess, meningitis, enteric fever, septic arthritis, osteomyelitis, and pneumonia, respectively. 7.5% (n=10) of the participants had Howell Jolly bodies. The duration of hydroxyurea splenomegaly was 0–5, 6–10, 11–15 years in 62.5% (n=30), 78.6% (n=44), and 71.4% (n=20 people). According to scintigraphy, 4.6% (n=6), 19.7% (n=26), and 75.7% (n=100) of the individuals had missing splenic function, impaired splenic function, and excellent splenic function, respectively (Table 2).

Splenic dysfunction and no dysfunction were observed in 4.1% (n=2) and 58% (n=28) of study participants with palpable spleens aged 0–5 years, and in 33.3% (n=16) of study participants with

non-palpable spleens, respectively. These findings are related to splenomegaly. In those with a palpable spleen aged 6–10 years, splenic dysfunction and no dysfunction were observed in 25% (n=14) and 53.5% (n=30) of the subjects, respectively, whereas in those without a palpable spleen, splenic dysfunction and no dysfunction were observed in 10.7% (n=6) of the subjects. In participants aged 11 to 15 years, splenic dysfunction and no dysfunction were seen in 14.2% (n=4) and 57.1% (n=16) of those with palpable spleens, respectively, and in 14.28% (n=4) of those without palpable spleens (Table 3).

Reticulocyte counts >4% were seen in 22 and 40 people with splenic dysfunction and no splenic dysfunction, respectively, with p=0.03, according to the research's findings about variables influencing splenic dysfunction in study participants. Reticulocyte count >4%, Hb <6 g/dl, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were statistically associated with significant splenic dysfunction (p=0.03, 0.002, 0.01, 0.02, 0.01, 0.01, 0.001, 0.001, and 0.01) (Table 4).

Reticulocyte count >4%, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, and other factors were significant predictors of splenic dysfunction in study participants with sickle cell disease, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years with p=0.03, 0.01, 0.01, 0.02, 0.001, and 0.03, respectively (Table 5).

DISCUSSION

Reticulocyte counts >4% were seen in 22 and 40 people with splenic dysfunction and no splenic dysfunction, respectively, with p=0.03, according to the research's findings about variables influencing splenic dysfunction in study participants. Reticulocyte count >4%, Hb <6 g/dl, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were statistically associated with significant splenic dysfunction (p=0.03, 0.002, 0.01, 0.02, 0.01, 0.01, 0.001, 0.001, and 0.01) (Table 4).

Reticulocyte count >4%, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, and other factors were significant predictors of splenic dysfunction in study participants with sickle cell disease. These findings were similar to those of earlier research by Lammers AJ et al. (2012) and George A et al, in which the authors evaluated participants using demographic information similar to that of the current study.

Regarding the study participants' illness data, 3% (n=4) had penicillin prophylaxis, and 100% (n=132) were immunized in accordance with the national vaccination schedule. Meningococcal, pneumococcal, and H. influenza B vaccinations were given to 7.6% (n=10), 12.1% (n=17), and 34.9% (n=46) of the patients in the optional vaccination history, respectively. Infections in 1.5% (n=2), 1.5% (n=2), 1.5% (n=2), 3% (n=4), 6% (n=8), and 7.5% (n=10) of the research participants were Hepatitis B, abscess, meningitis, enteric fever, septic arthritis, osteomyelitis, and pneumonia, respectively. 7.5% (n=10) of the participants had Howell Jolly bodies.

The duration of hydroxyurea splenomegaly was 0–5, 6–10, 11–15 years in 62.5% (n=30), 78.6% (n=44), and 71.4% (n=20 people). According to scintigraphy, 4.6% (n=6), 19.7% (n=26), and 75.7% (n=100) of the participants had normal splenic function, whereas the remaining subjects

had nonexistent or impaired splenic function. These disease features were comparable to those found in studies by Wang WC et al. (2011) and Abd El-Ghany SM et al, where the authors reported disease data comparable to the current study.

The findings of the study demonstrated that when evaluating the splenic dysfunction associated with splenomegaly in study participants from various age groups, 4.1% (n=2) and 58% (n=28) of study participants with palpable spleens and those without palpable spleens, respectively, Of the research participants, 4.1% (n=2) had splenic dysfunction, whereas 33.3% (n=16) did not. Splenic dysfunction and no dysfunction were seen in 25% (n=14) and 53.5% (n=30) of kids with palpable spleens aged 6–10 years, respectively, and in 10.7% (n=6) of patients with non-palpable spleens.

In participants aged 11 to 15 years, splenic dysfunction and no dysfunction were seen in 14.2% (n=4) and 57.1% (n=16) of those with palpable spleens, respectively, and in 14.28% (n=4) of those without palpable spleens. These findings were in line with research by Morrissey BJ et al. (2011) and Tewari S et al. (2012), who found that splenic dysfunction associated with splenomegaly was similar to what was seen in the current study.

Reticulocyte counts >4% were seen in 22 and 40 research participants with splenic dysfunction and those without splenic dysfunction, respectively, for variables influencing splenic dysfunction (p=0.03). Reticulocyte count >4%, Hb <6 g/dl, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were all associated with significant splenic dysfunction (p=0.03, 0.002, 0.01, 0.02, 0.01, 0.01, 0.001, 0.001, and 0.01; p=0.03, 0.001, 0.01, 0.01, 0.01, 0.01, 0.01, 0.01, 0.001, 0.001, 0.001, and 0.01). These results were consistent with those of investigations conducted by Dave K et al. and Colombatti R et al, Reticulocyte count >4%, Hb <6 g/dl, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years were documented as variables impacting splenic function in people with sickle cell disease (SCD) that are comparable to the current research.

The following factors were significant predictors of splenic dysfunction in sickle cell disease study participants: Reticulocyte count >4%, HbS levels >70%, not on hydroxyurea, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and age >5 years (p=0.03, 0.01, 0.01, 0.02, 0.001, and 0.03 respectively).

These results were consistent with research by Jain D et al. in 2020 and Ladu AI et al, wherein the authors found that the following factors independently predicted splenic dysfunction in subjects with SKD similar to the current study: age >5 years, history of >5 blood transfusions, history of >3 hospitalizations, history of >4 VOC, severe infection, and reticulocyte count >4%, HbS levels >70%, not on hydroxyurea.

CONCLUSION

It is possible to customize antibiotic prophylaxis for children from India who have a high prevalence of splenic dysfunction. In Indian children, the following criteria are independent of splenic dysfunction: HbS > 70%, reticulocyte count > 4%, children not taking hydroxyurea, > 5

blood transfusions, > 3 previous hospitalizations, > 4 vaso-occlusive crisis (VOC) episodes, and age > 5 years.

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S. No	Characteristics	Number (n)	Percentage (%)
1.	**Gender**		
a)	Males	64	48.4
b)	Females	68	51.5
2.	**Age group (years)**		
a)	1-5	48	36.3
b)	6-15	84	67.6
3.	**History**		
a)	Blood transfusion	98	74.25
b)	Severe infections	28	21.21
c)	Vaso-occlusive crisis	122	92.43
d)	Hospitalization	110	83.3
4.	**Presenting symptoms**		
a)	Stroke	4	6.06
b)	Breathlessness	18	13.64
c)	Chest pain	12	9.09
d)	Hematuria	6	4.55
e)	Anemia	48	36.3
f)	Jaundice	30	22.7
g)	Abdominal pain	46	34.8
h)	Fever	82	62.1
i)	Acute painful crisis	84	63.6

Table 1: Demographic data on study participants

S. No	Disease characteristics	Number (n)	Percentage (%)
1.	**Vaccinated as national immunization schedule**	132	100
2.	**Prophylaxis with penicillin**	4	3
3.	**Optional vaccination history**		
a)	Meningococcal	10	7.6
b)	H. influenza B	17	12.1
c)	Pneumococcal vaccine	46	34.9
4.	**Infection type**		

a)	Hepatitis B	2	1.5
b)	Abscess	2	1.5
c)	Meningitis	2	1.5
d)	Enteric fever	4	3
e)	Septic arthritis	4	3
f)	Osteomyelitis	8	6
g)	Pneumonia	10	7.5
5.	**Howell Jolly bodies present**	10	7.5
6.	**Hydroxyurea splenomegaly duration (years)**		
a)	0-5 (n=48)	30	62.5
b)	6-10 (n=56)	44	78.6
c)	11-15 (n=28)	20	71.4
7.	**Scintigraphy**		
a)	Absent splenic function	6	4.6
b)	Impaired splenic function	26	19.7
c)	Good splenic function	100	75.7

Table 2: Disease data in study subjects

S. No	Age years (n)	Spleen palpable				Spleen non-palpable			
		Dysfunction		No dysfunction		Dysfunction		No dysfunction	
		n	%	N	%	n	%	n	%
1.	**0-5 (48)**	2	4.1	28	58	2	4.1	16	33.3
2.	**6-10 (56)**	14	25	30	53.5	6	10.7	6	10.7
3.	**11-15 (28)**	4	14.2	16	57.1	4	14.28	4	14.28
4.	**Total (132)**	20		74		12		26	

Table 3: Splenic dysfunction related to splenomegaly in study subjects from different age groups

S. No	Variables	Splenic dysfunction	No splenic dysfunction	p-value
1.	**Reticulocyte count >4%**	22	40	**0.03**
2.	**Hb <6 g/dl**	24	30	**0.002**
3.	**HbS levels >70%**	20	26	**0.01**
4.	**Not on hydroxyurea**	24	40	**0.02**
5.	**History of >5 blood transfusions**	12	10	**0.01**
6.	**Splenomegaly**	20	74	0.26
7.	**History of >3 hospitalization**	18	26	**0.01**
8.	**History of >4 VOC**	24	28	**0.001**
9.	**Severe infection**	14	14	**0.001**
10.	**Age >5 years**	28	56	**0.01**

Table 4: factors affecting splenic dysfunction in study subjects

S. No	Parameters	Number (n)	Percentage (%)	Adjusted OR (95% CI)	p-value
1.	**Reticulocyte count >4%**	22	68.73	3.376 (1.036, 10.992)	**0.03**
2.	**Hb <6 g/dl**	24	75	1.843 (0.524, 6.463)	0.31
3.	**HbS levels >70%**	20	55.55	4.485 (1.383, 14.575)	**0.01**
4.	**Not on hydroxyurea**	24	75	4.11 (1.22, 14.15)	**0.01**
5.	**History of >5 blood transfusions**	12	37.5	4.131 (1.203, 14.174)	**0.01**
6.	**Splenomegaly**	20	55.55	0.584 (0.176, 1.897)	0.38
7.	**History of >3 hospitalization**	18	56.25	3.517 (1.103, 11.237)	**0.02**
8.	**History of >4 VOC**	24	75	6.990 (1.990, 24.547)	**0.001**
9.	**Age >5 years**	28	87.5	4.577 (1.041, 20.095)	**0.03**

Table 5: Prediction of splenic dysfunction in study subjects with sickle cell disease